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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/180,209 12/22/99 KARPUSAS

M B189

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HM12/0410

EXAMINER

MORAN, M

ART UNIT	PAPER NUMBER
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1631

DATE MAILED:

04/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/180,209

Applicant(s)

KARPUSAS ET AL.

Examiner

Marjorie Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12 and 38-40 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 12, 40 and 48 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

All rejections and objections not repeated below are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the signature of Inventor Singh is not dated.

Specification

The abstract of the disclosure is objected to because it is not directed to the subject matter of the pending claims. Appropriate correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

Claim 12 is again rejected, as previously set forth in the office action of 9/26/00 and new claims 38-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a computer readable storage medium or machine comprising such a medium, wherein the medium comprises data capable of displaying a three-dimensional (3D) representation of a crystal of residues 116-261 of human cD40

Art Unit: 1631

ligand (CD40L), does not reasonably provide enablement for a machine or medium comprising data for displaying a crystal of any CD40L complex, non-human CD40 ligands, full-length CD40 ligands, mutants or variants of any CD40 ligand, or any CD40L fragment other than residues 116-261.

Applicant's arguments filed 1/3/01 have been fully considered but they are not persuasive. In response to applicant's argument that the specification discloses a method for crystallizing and obtaining structure coordinates for CD40 ligand proteins and provide an example thereof, it is noted that the specification exemplifies a method of crystallizing and obtaining structure coordinates for ONLY residues 116-261 of a human CD40 ligand (p. 33, Example C). No examples or coordinates are disclosed for crystals of any complex of CD40L or fragment of CD40 ligand with any other molecule, nor for a full-length CD40L nor for a full-length or fragment of a non-human CD40L nor for any variant or mutant of a CD40L or fragment thereof. Although the specification states on page 7 that the disclosed crystal structure can "be used to solve" crystal structures of mutant or homologous CD40L molecules, or of fragments or co-complexes or CD40L, the specification does not specifically disclose how to do so. The applicants admit, on page 4 of the specification, that merely knowing a sequence of a compound does not allow an accurate prediction of the crystal structure of a protein or ligand. In addition, it is known in the art that a change in a single residue can be sufficient to significantly perturb a protein's structure and function (e.g. substituting a proline for a residue in a alpha helix may cause a "kink" such that the helix can no longer form). The specification discloses neither a sequence nor a crystal for any CD40L or fragment

Art Unit: 1631

or complex thereof other than residues 116-261 of human CD40L. Applicant's argument that intracellular and transmembrane domains do not bind CD40L is germane only insofar as these domains are part of a full-length CD40L, therefore the sequence (and structure) of these domains would be expected to contribute to the crystal structure of the CD40 binding domain in the full-length protein. Any perturbation in the sequence or structure of these domains would also be expected to perturb the crystal structure of the binding domain in the full-length protein, therefore knowing the crystal structure of an isolated binding domain does not necessarily predict the crystal structure of a full-length protein, of any other domain, or of the binding domain as part of a full-length protein which is a mutant or variant of CD40L.

Applicants appear to be confused about the scope of the claims. The claims recite "a crystal of a molecule or molecular complex comprising a fragment of a CD40 ligand having a binding site for CD40 comprising" particular amino acids. The term "comprising" is open claim language, therefore a "crystal of a molecule or molecular complex comprising a fragment of a CD40 ligand" is not limited to a fragment ONLY, but also encompasses a crystal or complex comprising any part of a CD40 ligand, up to and including the full-length protein. It is assumed that it is "the fragment" which is limited to "have" a binding site for CD40. The term "having" is also interpreted to be open claim language, therefore a "fragment having a binding site for CD40" is not limited to the fragment which is the binding site for CD40 (residues 116-261?), but also encompasses ANY fragment of any size, as long as that fragment includes the CD40 binding site (e.g. the claim encompasses a fragment comprising residues 1-300, or a fragment

Art Unit: 1631

comprising both a CD40 binding domain and a transmembrane domain). While both the fragment and the binding domain are limited to comprise particular amino acids, and the data on the storage medium is limited to comprise structure coordinates for particular amino acids, it is again noted that "comprises" and "comprising" are open claim language, therefore the fragment, binding domain, and data may include more than the recited residues.

As a crystal structure for a CD40L complex is specifically recited in the claims, but is not enabled by the specification or prior art, the claims are not enabled for a medium or machine comprising data capable of displaying a crystal structure of a molecular complex comprising any part of any CD40 ligand. As a crystal structure for non-human CD40 ligands, variants of CD40 ligands, full-length CD40 ligands, and fragments of CD40 ligands other than a fragment consisting of residues 116-261 of human CD40L are encompassed by the claims but are not enabled by the specification or the prior art, the claims are not enabled for a medium or machine comprising data capable of displaying a crystal of any CD40 ligand or fragment thereof other than a fragment of human CD40 ligand consisting of residues 116-261. For the reasons previously set forth and set forth above, claims 38-40 are rejected and the rejection of claim 12 is maintained.

Claims 12 and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 12 and 39-40 recite structure coordinates of specified amino acids "according to Table 1". Recitation of a Table or graph in the specification renders the claims indefinite as it is unclear what limitations are intended to be incorporated in the claims. See 2173.05(s). It is unclear whether applicant intends to include all of the coordinates disclosed in Table 1 in the claims, or only coordinates Lys143, Arg203, Ard207, and Tyr145. In addition, multiple coordinates are recited for each amino acid. If applicant intends only the coordinates for the specified amino acids to be incorporated into the claims, then it is further unclear if applicant intends all of the coordinates for each, or only particular coordinates (e.g. those coordinates which correlate with a particular conformation of the protein). For these reasons, the claims are indefinite.

Applicant's arguments filed 1/3/01 have been fully considered but they are not persuasive. In response to applicant's argument that the amino acids are taught in Table 1, it is noted that reference to a Table in the specification does not render the claims definite, as set forth above. Applicant should note that recitation of particular amino acids (e.g. Lys143) may be made definite by reference to the amino acid in a particular SEQ ID NO.

Conclusion

Claims 12 and 38-40 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703)


Application/Control Number: 09/180,209

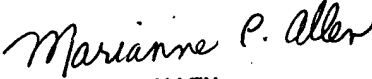
Page 8

Art Unit: 1631

308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524.


Marjorie A. Moran
April 9, 2001


MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1800~~
Au (63)